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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/740,288	12/19/2000	Stephen M. Allen	BB1429 US NA	8577

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EXAMINER	
WALICKA, MALGORZATA A	

ART UNIT	PAPER NUMBER
1652	10

DATE MAILED: 04/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/740,288	ALLEN ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9-15,21 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2-5* is/are allowed.

6)☒ Claim(s) *1,9-15,21 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Reasons for allowable subject matter, copy of sequence search, copy of article by Weaver et al.

The examiner acknowledges Amendment and Response to Restriction Requirement filed on February 20, 2002, paper No. 9. The amendments to the claims have been entered as requested. Claims 6-8, 16-20, 22 and 23 are cancelled. Claims 1-5, 14, 21, are amended. New claims 24-26 are entered. In response to restriction requirement, Paper No. 7, Applicants elected Group I drawn to polypeptides encoding biotin synthase. In response to requirement of plant species election Applicants elected maize, SEQ ID NO: 21-24. Claims 1-5, 9-15, 21 and 24-26 are pending in the application and are the subject of this Office Action.

DETAILED OFFICE ACTION

This application claims the benefit of U.S. provisional application No. 60/172,929 filed on December 21, 1999. The provisional application contains only partial amino acid sequences elected by Applicant for prosecution in the instant application. SEQ ID NO: 6 of the provisional application contains 95 initial amino acids of SEQ ID NO: 22, whereas SEQ ID NO: 8 of the provisional application contains 340, and not 377 amino acid of SEQ ID NO: 24. The priority date of the claims pending in the instant application is, therefore, its filling date, December 19, 2000.

1. Objections

1.1. Specification

The specification is objected to for a vague definition of percent identity of nucleic acid molecules given on page 8, line 23. "Substantially similar nucleic acid fragments of the instant invention may be characterized by the percent identity of the amino acid sequences that they encode to the amino acid sequences disclosed herein, as determined by algorithms commonly employed by those skilled in this art." Those skilled in the art realize that algorithms commonly employed may give different results. Calculations of percent identity depend on parameters' values chosen for calculations. Choosing of these values particularly influences comparison of sequences having close percent identity. Applicants used for their determinations LASEREGENE computing suite. On page 8, line 37 and page 26 line 5 Applicants write "Sequence alignments and percent identity calculations were performed using the Megalign program of the LASEREGENE bioinformatics computing suite (DNASTAR Inc., Madison, WI)." However Applicants are silent about parameters' values used for calculations. Applicants only quote the default parameters used for the Clustal method of alignment (GAP PENALTY =10, GAP LENGTH penalty =10).

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicant may become aware.

1.3. Drawings

This application has been filed with informal drawings, which are acceptable for examination purposes only; see the attached PTO Form 948. Formal drawings will be required when the application is allowed.

2. Rejections

2. 1. 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 1 and dependent claims 9-15, 21, and 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regard as the invention.

Claim 1 recites the phrase "at least 85% sequence identity based on the Clustal alignment method." The definition of the percent identity given by the claim is vague because the Clustal method of alignment is used to align sequences and not to calculate the percent of identity. Applicants set forth, on page 8 and 26; see the above objection to the specification, that percent identity was calculated using the Megalign program of the LASEREGENE bioinformatics computing suite (DNASTAR Inc., Madison, WI)," but Applicants do not disclose the parameters chosen for these calculations. Therefore, the term 85% identity is indefinite and makes the claim indefinite.

Claim 14 is indefinite because it recites in preamble and part (b) indefinite phrase "a nucleic acid molecule" and in part (a) "a polynucleotide of Claim 1." It is, therefore,

not know to what polynucleotide the claim is directed. Besides, step (a) includes the term "selecting" which is confusing, because it is not an active step in the method. Furthermore, the phrase "containing the nucleotide sequence" in step (b) is unclear, because it is neither an open language "comprising the nucleotide sequence" nor the closed language "consisting of the nucleotide sequence." Dependent claim 15 is included in the rejection, because it does not correct the deficiencies of the claim from which it depends.

Claim 26 is directed to a method for isolating a polypeptide encoded by the polynucleotide of claim 1, wherein said method comprises only one step, i.e. isolating said polypeptide. The claim is confusing because this step is a repetition of preamble, and the claim does not set forth any specific steps in the chemical process of the polypeptide isolation. For that reason it is not clear whether Applicants mean the process of chemical isolation of said polypeptide or its recombinant production.

2.2. 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2.2.1. Lack of written description

Claims 1 and dependent claims 9-15, 21 and 24-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter, which was not described in

the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to a polynucleotide encoding biotin synthase that is at least 85% identical to SEQ ID NO:22 or 24.

The scope of the claims covers a large variable genus of polynucleotides. The Claims and the specification do not provide **structural characteristics** of the claimed polynucleotides with exception of that of SEQ ID NO: 21 and 23 encoding two natural variants of the maize biotin synthase. This is however not sufficient to put in possession of one skilled in the art the attributes necessary to make the claimed invention. The specification fails to describe any other representative species of the polynucleotides enumerated in claim 1 by any identifying characteristics or properties other than that it is to be a biotin synthase and 85% identical to SEQ ID No:22 or 24. Neither the claims nor the specification provide the structure of the claimed polynucleotides. In view of lack of specific structural characteristics of claimed polynucleotides Applicants failed to sufficiently describe the claimed invention in such full, clear concise, and exact terms that a skilled artisan would recognize they were in possession of the claimed invention.

2.2.2. Scope of enablement

Claims 1 and dependent claims, 9-15, 21 and 24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO:21 and 23 encoding two natural variants of the

maize biotin synthase, does not reasonably provide enablement for any polynucleotide, from any biologic and man made source, having a biotin synthase activity and 85% identity to SEQ ID No: 22 or 24. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to the extremely large number of polynucleotides that are claimed in claim 1 as set forth above in the rejection for lack of written description.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompass any polynucleotide from any biologic or man made source encoding the polypeptide that is at least 85% identical to SEQ ID NO: 22 or 24 and has activity of the biotin synthase.

While methods of gene isolation, gene structure manipulations and determination of biotin synthase activity are known in the relevant art, and skills of the

artisans highly developed, it is not a routine in the art to isolate, from any organism and man-made library, polynucleotides that encode polypeptides having at least 85% identity with SEQ ID NO: 22 or 24, make measurements of their biotin synthase activity and further to select those that have biotin synthase activity. The only example provided by disclosure are the polynucleotide of SEQ ID NO: 21 and 23 encoding natural variants of the biotin synthase of maize. Examiner concludes that without the further guidance on the part of Applicants in regards of the structure and source of the claimed polynucleotides, experimentation left to those in the art is improperly extensive and undue.

2.3. 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 and dependent claims 9-15, 21 and 24-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Weaver et al. (Characterization of the cDNA and gene coding for the biotin synthase of *Arabidopsis thaliana,* Plant Physiol. 1996, 110:1021-1028, included in the Information Disclosure Statement). The claims are directed to the nucleotide sequence encoding a polypeptide having biotin synthase activity wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO: 22 or 24 have at least 85% sequence identity based on the Clustal alignment method.

Weaver and co-workers disclose the biotin synthase of *Arabidopsis thaliana* that is in 89.7% and 89.1% identical to SEQ ID NO:22 and 24, respectively; see enclosed copy of the sequence search.

4. Conclusion

The application contains the allowable subject matter. The following is a statement of reasons for the indication of allowable subject matter:

Applicants disclose novel DNA molecules of SEQ ID NO: 21 and 23 that encode plant biotin synthase variants SEQ ID NO:22 and 24, obtained from maize. There is no prior art for biotin synthase from this plant. The closest prior art concerns the enzyme from Arabidopsis Thaliana; see the article used in rejection under 35 U.S.C. 102, made in this Office Action. Biotin is an important molecule that serves as a cofactor that covalently binds to carboxylases and facilitates the transfer of carboxyl group during enzymatic reaction involving carboxylation, decarboxylation and transcarboxylation. Plant biotin genes have potential use as targets for herbicidal treatment.

As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

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